

THORNER (M.)

Compliments of the Author.

SALOL:

WITH REPORT ON THE USE OF SALOL IN AFFECTIONS
OF THE THROAT, EAR AND EYE.

BY

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OF CINCINNATI.



[Read before the Cincinnati Academy of Medicine, November 14, 1887.]

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191

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WITH REPORT ON THE USE OF SALOL IN AFFECTIONS OF THE THROAT, EAR, AND EYE.

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SALOL, the salicylate of phenol, was introduced into therapeutical use by Von Nencki and Sahli of Berne, Switzerland, about 18 months ago. They tried to find a remedy, which being free from the objectionable features which so often attend the use of salicylic acid and its sodium salt, would possess the same or similar medical properties. Since the first publication of Sahli⁽¹⁾, in which he strongly recommended the new remedy, it has been used by a number of observers in the treatment of a host of different affections, and the results, so far as published, were encouraging enough to warrant further trial. The experience which I have had with salol is limited. Nevertheless, I undertake to report my results to you, because I deem it proper, to add to our knowledge as to the value or non-value of a new remedial agent by bringing before you for discussion the question of the therapeutical action of this drug. And from this standpoint every additional report regarding the action of a new, and comparatively little known drug, may help to settle the pending investigation, whether the new remedy shall find a place in our daily armamentarium or not. "In an inquiry of this kind," to use the words of the late S. D. Gross, "in fact, individual experience amounts to nothing; collective experience is everything."

Salol, the salicylate of phenol, is a derivative of salicylic acid, in which one atom of hydrogen is replaced by the phenol group. The drug contains 60 per cent. of salicylic acid, and 40 per cent. of carbolic acid. It is a white powder, crystallizing in small scales, is almost insoluble in water,

but soluble in alcohol, ether, petroleum ether, fatty oils. It is nearly tasteless, and has a decided aromatic odor, which latter, though not very strong, is easily perceptible. In the organism salol undergoes, according to Prof. Von Nencki, a simple splitting up into its two components. This decomposition takes place in the duodenum, and not in the stomach, the drug being only soluble in the pancreatic juice, as Von Nencki found in his first experiments. Sievers and Ewald⁽²⁾, however, found, that the pancreatic juice is not required for the decomposition of salol, but that all parts of the intestinal tract, except the stomach, have the power of splitting salol into its components, since it is readily decomposed in any alkaline solution in body temperature within a short time. Thus it was found in the urine $\frac{3}{4}$ to 4 hours after being introduced into the rectum in an enema or in a suppository. On the other hand the acid reaction of the gastric secretion prevents the decomposition of salol. This was proven by the following two experiences. A dog, whose pylorus was doubly ligated, and into the stomach of which 1 gramme of salol was introduced with the aid of the stomach sound, did not excrete salicylic acid in his urine. In the other experiment the gastric juice was rendered alkaline by large doses of bicarbonate of sodium, and salol was then given. The result was that the salol decomposed in the stomach, as shown by the examination of the expressed contents of the stomach. Sahli has of late ⁽³⁾ demonstrated that salol is also decomposed by the saliva, although in a very slight degree, by dead organic matter, and by the action of bacteria.

Salol, after being decomposed in the



intestinal tract, soon appears in the urine as salicyluric acid and sulphocarboic acid. (4), In many cases the urine shows twenty-four hours after the introduction of the salt the discoloration characteristic of the presence of phenol, changing from a slight greenish brown to dark olive green and even to black in the following days. This discoloration remains in a number of cases for several days after discontinuing the drug; in some it disappears whilst the drug is still being used. There are, however, cases where this discoloration does not take place at all or in an exceedingly slight degree. The presence of the salicylic acid in the urine is ascertained much sooner by the chloride-of-iron test. Two hours after the first dose being taken a violet color is developed by adding a few drops of the test solution to the urine.

Sievers and Ewald (5) state, that this salicylic acid reaction may be found as early as from 30 to 60 minutes after the administration of small doses of salol. In order to show this early reaction it is necessary to previously acidulate the urine with hydrochloric acid, and to shake it then well with ether, when the addition of the chloride-of-iron solution will produce the violet tint.

As to its therapy, salol has proven to be a very valuable remedy in a number of diseases, in which salicylic acid has been used to good effect. This is not surprising, when we consider that it affords us an easy means of introducing large doses of salicylic and carboic acid into the system. "The effects of the salicylic acid" says Bartholow (6), "are increased in all directions by the members of the phenol group." The properties of salol may be conveniently termed:

Antirheumatic and Antineuralgic;
Antifebrile;
Antiseptic.

Sahli treated (7) a number of cases of acute and subacute articular rheumatism with it, and experienced splendid results. He gave it in doses of thirty grains three and even four times a day. He furthermore used it in neuralgias of different kinds, in erythema nodosum and multiforme, urticaria and peliosis, in all of which affections it was evidently of decided benefit.

Other observers have confirmed the efficacy of salol in all affections of rheumatic origin. Thus Bielschowsky (8) treated

twenty-seven cases of acute articular rheumatism with salol in doses of seventy-five grains *pro die* within five hours, or of two drachms within eight hours. In nineteen out of these twenty-seven cases a perfect cure was obtained, in two cases salol had but little effect, and resort to the use of salicylic acid was necessary in order to effect a perfect cure. In six cases neither salol nor salicylic acid were able to prevent the cases from ending in the chronic form. In eight cases relapses occurred, from which, however, they recovered after smaller doses of salol. The average quantity which a single patient received during the treatment was five and a half drachms (twenty-two grammes), the largest dose being ten and a half drachms (forty-two grammes), the smallest being three and one-fourth drachms (thirteen grammes). The time necessary for effecting a cure was usually four to eight days.

Dr. S. Rosenberg (9) reported that salol given in doses of from one and a half to two drachms (six to eight grammes) *per die*, in single doses of fifteen grains, had in cases of acute articular rheumatism generally a good effect, the longest time necessary to abate pain and fever being five days, while in most cases twenty-four to forty-eight hours were required. In one case it was necessary, after a failure with salol, to fall back on salicylic acid, which had the desired effect within twelve hours. He also found that relapses and complications with heart affections were not entirely missing.

Another observer, Dr. Georgi, (10) is full of praise of salol as an antirheumatic and antineuralgic. He saw splendid results following its use in acute articular rheumatism in doses of one and a half drachms (six grammes) *pro die*, especially in the acute form; furthermore, in different neuralgias, and in muscular rheumatism, though in the latter the good effects were less pronounced. In only three out of twenty cases of acute muscular rheumatism treated with salol relapses set in, the appearance of which were usually prevented by continuing the use of smaller doses of salol (viz.: fifteen grains three times a day) after the acute symptoms had entirely subsided.

Herrlich (11) used salol in Leyden's clinic in Berlin, in cases of acute articular rheumatism, and in different forms of muscular rheumatism, lumbago, etc., and he also

stated that the results obtained were exceedingly satisfactory. One and a half drachms (six grammes) of salicylic acid did not produce the same prompt action of corresponding doses of salol. Relapses and endocarditic complications were uninfluenced by it.

Out of the number of other of other observations, which all bear evidence to the good effects of salol in rheumatic and neuralgic affections, only one more may be mentioned. Dr. v. Aschenbach⁽¹²⁾ of Corfu, suffering from severe attacks of sciatica, took seven grains in the evening and fifteen grains at midnight, when he fell asleep and remained perfectly free from pain.

In addition to the good effects of salol in alleviating pain and swelling in rheumatic and neuralgic affections, the antipyretic action of the drug has been claimed to be a considerable one. According to most of the observers named above, the temperature fell in cases of acute articular rheumatism soon after the introduction of the drug, corresponding with the subsidence of pain and swelling. There are furthermore observations which tend to show that salol may be used advantageously in acute infectious diseases, also as an antipyretic. It is in the first line Georgi⁽¹³⁾ who recommends salol for acute febrile diseases. He used it in cases of phthisis, of very acute peritonitis, and of erysipelas of the face, and observed that from $22\frac{1}{2}$ grains to 45 grains were in all cases sufficient to reduce the temperature. In many cases smaller doses, repeated at shorter intervals, had also a beneficial effect.

Other observers do not give so much prominence to the antipyretic properties of salol, and Lépine⁽¹⁴⁾, of Lyons, found that the temperature reducing action of salol in typhoid fever was not so pronounced as that of antipyrine.

The antiseptic action of the remedy has been made use of for a great variety of different diseases. Sahli⁽¹⁵⁾ himself used it with good results as a dusting powder in syphilitic and other ulcers, which were rapidly healed under its use, and in ozæna and otorrhœa; besides, as a three per cent. mouth wash, and as an emulsion for injection in gonorrhœa. He reported of late⁽¹⁶⁾ also the use of salol in gauze bandages for tamponing the vagina, and for insufflation of a powder consisting of salol and talcum in the relation of 1-1 and 1-3 for erosions of the cervix. But in this respect, espec-

ially as a powder for insufflations, salol has hardly any advantage over many of our old preparations, while the disadvantages must not be underestimated. Sahli himself admits that salol is not easily reduced to a fine powder, and even when so converted it readily balls again together. After the addition of substances like talcum, lycopodium, etc.; or amyllum, it is said to form a better powder. But that such a powder does not meet our requirements for local applications when we want an impalpable powder, as, for instance, in insufflations into the respiratory tract or into the ear, is evident. And Seifert⁽¹⁷⁾ of Wurzburg, was, on account of these causes, dissatisfied with the application of pulverized salol in affections of the nose. He, however, found it to be very effective as a mouth wash in ulcerative processes of the mouth and throat, also in diphtheria. As a mouth wash, in fact, it is recommended for quite a number of affections. Georgi used it in angina lacunaris and catarrhalis, with the same effect as chlorate of potash, in a moderate case of diphtheria, in stomatitis mercurialis, and for deodorizing the mouth in typhoid fever, with good results.

The antiseptic properties of salol have further been made use of by Georgi⁽¹⁸⁾ and by Feilchenfeld⁽¹⁹⁾ in cases of pyelitis and cystitis. With doses of 30 to 45 grains *pro die* the latter had brilliant success, the urine apparently being prevented from undergoing alkaline decomposition by the salicylic and carbolic acid contained in it. In one case of phagedænic chancre which had resisted every effort of treatment, a cure was soon effected after salol as a dressing powder had been resorted to. Perier and Patein⁽²⁰⁾ have used it as a substitute for iodoform as a surgical dressing, and were very favorably impressed with the results obtained therewith. Sahli and others recommended salol also for phthisis, in small doses, and in intestinal catarrh, dysentery, typhoid fever and even cholera. They concluded that the salicylic and phenic acid rendered free in the intestines by the decomposition of salol might act, if not as a disinfectant, still as preventing further development, and in fact favorable results have been recorded in a number of cases. Thus Georgi relates that in a case of typhoid fever the appearance of the tongue changed rapidly after the use of salol, for the better, and the patient felt "tolerably

well," and the whole disease seemed to be beneficially influenced. Cases of intestinal catarrh were cut short by others after they had been treated only a short time with salol. Yet Sahli himself in his last publication⁽²¹⁾ that though salol possesses under certain circumstances certainly high antiseptic properties, the decomposition into salicylic and carbolic acid being effected by the bacteria and living tissues; yet this drug is inferior to the same amount of salicylic and carbolic acid as an antiseptic. Also, according to Pinet⁽²²⁾ the antiseptic properties of salol are far below those of salicylic acid. And Herrlich⁽²³⁾ found no specific action in acute infectious diseases, especially in typhoid fever; intestinal complications, which eventually were present, seemed not to be influenced by it.

Thus far the therapeutical actions only of salol have been spoken of, without reference being made to any untoward symptoms which might be exhibited after the administration of it. There is a general agreement of nearly all observers as to the absence of any disturbing action of the drug on the gastric mucous membrane, because of its being insoluble in the gastric secretion. It was, according to the majority of writers on this subject, always well borne by the stomach, and nausea, vomiting, and gastric distress were absent. No other unpleasant accessory effects, which we so frequently see after the use of salicylic acid, except occasionally slight noises in the ears, were reported to follow the use of salol in the doses mentioned above. There are differences of opinion, however, on this point. Thus, Herrlich⁽²⁴⁾ noticed ringing in the ears, gastric disturbances in patients in a very weak condition, congestion of the brain, and chills. In one patient with chronic articular rheumatism, who had taken six drachms (24 grammes) of salol within three days, severe symptoms of carbolic acid poisoning occurred. She vomited almost incessantly for eight days and had much pain and difficulty in passing water. Similar urinary troubles were observed in another case. Rosenberg⁽²⁵⁾ saw almost all the unpleasant accessory effects as after the salicylate of sodium. They appeared, however, less severe, and the stomach seemed to be less irritated. Even Georgi, the most enthusiastic of all clinicians, who wrote on salol, admits of its not being entirely free from unpleasant after-effects. He noticed in a

few cases severe buzzing in the ears, and in one case, where two drachms (eight grammes) of salol had been swallowed within a short time, symptoms of slight poisoning, viz., excessive vomiting, pain in gastric region, and intense tinnitus-aurium.

The mode of administration of salol is the following: It may be given in powders of 5-15 grains, which in most cases are swallowed without difficulty. If the odor be objectionable, you may give it with the addition of some oil of peppermint, as recommended by Sahli⁽²⁶⁾; or in capsule, pill, or compressed tablet. Sahli recommends to add in the latter form very small quantities of starch, in order to facilitate the rapid disintegration in the intestinal canal, which in some cases did not take place, the tablets leaving the body with the feces. As a mouth-wash, it is used in 3 to 6 per cent. alcoholic solution; of this, add about half a teaspoonful to half a glass of warm water and use it at once. As a powder for dressing wounds and insufflations, it is best combined with amylum in 1 to 10 per cent. strength. Or it may be used in oily solution or in salve form in the same percentage⁽²⁷⁾. Furthermore⁽²⁸⁾, four parts of salol being dissolved in four parts of ether, may be combined with thirty parts of flexible collodion; or it may be used in the form of a liniment for burns, one part to six equal parts of olive oil and lime water; or in suppositories.

The foregoing extracts from medical literature contain about that, in brief, which has been written to this date about salol. The report of cases which I am to add will be limited to affections of the throat, ear, and eye. These cases, however, belong to the same class of affections in which most other observers recorded good results, viz., affections of *rheumatic* or *neuralgic* origin.

I.—THROAT AFFECTIONS TREATED WITH SALOL.

In four cases of acute catarrhal pharyngitis, especially in that form, which, occurring in patients of a rheumatic diathesis, has been termed rheumatic angina, salol had a decided beneficial influence. When given in doses of 10 to 15 grains three times a day, the pain in the throat and neck disappeared rapidly; after two doses patients were able to swallow, and the following day no other symptoms were pres-

ent than slight redness of the fauces. No other internal or external applications, except a wet pack around the neck, were made, and no other symptoms appeared after pain in the throat had disappeared.

In tonsillitis follicularis the action was not so rapid, but in these cases, also, great benefit was derived from the use of this remedy. A boy, *æt.* 10, with a severe attack of follicular tonsillitis, the tonsils nearly touching each other in the median line, was given 10 grains at noon and 10 grains at bed-time. In addition, he used a simple Listerine gargle and took a saline aperient. After the second dose the pain was so diminished that he was able to swallow; but becoming very restless, and complaining of much pain again towards midnight, his mother gave him a third dose of 10 grains, after which he soon became quiet and went to sleep. The improvement continued the following day, so that he was towards evening nearly free from pain; the tonsils, though still showing some white spots, were decidedly smaller; and the submaxillary glands, previously very much enlarged and tender to the touch, were diminished in size considerably. At bed-time he received another dose of 10 grains, had an excellent night, after which recovery soon took place. In two other cases of follicular tonsillitis the pain grew rapidly less after the internal use of salol, and the restlessness towards night, which is so common in this affection, soon disappeared.

The latter effect was noted very often after the use of salol, especially in three cases of parenchymatous tonsillitis, where an abscess had formed when the patients were first seen. In one case, where incision was refused, 15 grains of salol three times a day, combined with warm applications, relieved the patient so much that she was able to sleep, which she was unable to do the two previous nights. And this relief continued the following day, under the use of salol, until spontaneous opening of the abscess occurred. In another case of quinsy, the patient was a very weak lady, prostrated from high temperature and loss of sleep during the last three days, in which time she had hardly taken any food. She found considerable relief from a deep incision into the tonsil, following which there was a free escape of pus. This was done at noon. Towards evening the patient complained again of much pain and restlessness. She insisted upon receiving

some hypnotic, since she did not feel able to stand another sleepless night. I ordered salol in powders of 10 grains each, and left a prescription for chloral hydrate. The directions were to take one powder of salol, and after one hour another. If, after this, the pain should not cease, the second prescription, calling for chloral hydrate, was to be made use of. The effect of the salol was marvelous. About one-half hour after the second dose the patient had no more pain, and slept all night. Recovery was prompt.

In three cases of torticollis rheumaticus the effect of salol was very pronounced. The first case was that of a gentleman, whom I treated for a subacute otitis media purulenta, and who presented himself one morning in February last with a typical wry neck, so that he was not able to move his head. I ordered pills, containing five grains of salol, every two hours. He began taking the pills at 11 a.m., and repeated this dose at 1 and 3 p.m., when he was able to move his head tolerably well, and felt nearly free from pain. He then discontinued taking the pills until 7 p.m., when he noticed again some stiffness and pain in his neck. He then took five grains; and at 9 p.m., when he went to bed, feeling still great inconvenience in putting his head on his pillow, he took 10 grains. He awoke the next morning perfectly free from pain and stiffness in the neck. A few more doses of five grains were ordered to prevent a repetition of the attack. No other treatment of whatever kind was exhibited. In the two other cases of rheumatic wry neck which I treated with salol, the result was similar.

As a local application I have used salol only as a mouth-wash, in a 6 per cent. alcoholic solution in cases of stomatitis mercurialis, in syphilitic ulcers of the pharynx, and in ulcers of the tongue from the irritation produced by the sharp edge of a tooth. But I failed to find any advantage over other local applications heretofore used.

II.—EAR AFFECTIONS TREATED WITH SALOL.

Two cases of otalgia nervosa, existing only a short time and without any objective sign of disease, were treated with 10 grains of salol, to be repeated every three hours. After the third dose the pain was gone in each case.

In two out of three further cases of ear affections, treated by Dr. Joseph Aub, of this city, to whom I am indebted for the report, salol had a very satisfactory result. One, a case of simple otalgia nervosa, was relieved after the first dose of 10 grains of salol, although the patient persisted in the use of the drug for three days following. In the second case, a case of chronic otitis media purulenta, the patient, suffering from persisting shooting pains in and behind the ear, was relieved after using the remedy for two days in doses of 10 grains three times a day, and has had no recurrence of the pain since (about six weeks). The third case was one of severe neuralgia of the entire head, especially located in both ears. In this case salol afforded no relief, although continued for over a week in doses mentioned above. The subsequent treatment with the constant current and Grosser's neuralgia pills gave full relief.

III.—EYE AFFECTIONS TREATED WITH SALOL.

The following cases were partially treated by me whilst taking charge of Dr. Aub's practice during this summer, and partially by Dr. Aub himself, who has kindly furnished me with the histories:

Two cases of simple ciliary neuralgia of long standing, one of which had been under treatment for many years, were treated with salol. The first case, of shorter duration, was relieved after the exhibition of the third dose; the second case, of longer standing, resisted the remedy for four days; then relief was gradually obtained and, after the remedy had been used in three daily ten-grain doses for a week, the patient was entirely free from pain, and has had no return of the pain for the last four weeks. This patient has suffered from these pains for over twenty years, the pains being so severe as to confine her to her bed on an average three days out of every week.

In two cases of rheumatic iritis, in which persistent ciliary neuralgia existed, the remedy was also used. In the one case the salicylate of sodium had been used with good effect; it was discontinued on account of its gastric disturbances and salol substituted with great benefit. In the other case the drug was used from the beginning, and checked the pain after the first dose.

In one case of acute catarrhal conjunctivitis, combined with severe supraorbital pain, which relapsed for months in spite of the internal administration of the salicylate of sodium, salol was also given. The salicylate of sodium was discontinued on account of its producing severe tinnitus aurium and deafness, though it never failed to relieve the neuralgia. The result after the use of salol was as well a rapid as a permanent one, the remedy having been continued for one week, without ever producing the annoying complications on part of the ear, which had deterred the patient from a continued use of the salicylate of sodium.

In one case of acute trachoma with ulcerative pannus, in which the pain over and around the eyes was so intense that the patient had been compelled to use hypodermatic injections of morphia daily to procure rest, salol was given in ten-grain doses three times a day. The effect was marvelous. After a few doses patient felt tolerably well, but would be awakened in the night with the severe pain, and after taking one dose of ten grains fell asleep within thirty minutes. This prompt action caused the nurse attending this patient to speak of the remedy as a hypnotic. The repetition of the drug during the day was discontinued after three days, and only one dose was given at bedtime, eventually to be repeated during the night whenever a sudden onset of pain caused sleeplessness. The remedy was used in this manner, with the effect of relieving pain and producing quiet sleep, for two weeks, when it was only used whenever patient noticed an approach of the pain, which, however, seldom occurred.

In most of these cases of throat, ear, and eye affections the dose was ten grains three to four times a day till relief was obtained. In some cases the single dose was 15 grains, in others the ten-grain dose was repeated after one hour. At times the patient was ordered to take the remedy whenever indicated by pain. No unpleasant effects were ever observed to follow the use of salol, except slight ringing in the ears in two cases, where the single dose was 15 grains. But you will have noticed that in the cases reported by me, the quantity of salol given within 24 hours was rarely, if ever, larger than 40 grains, which is by far less than the doses usually administered. These small doses of 10 or 15

grains of salol were mostly sufficient in cases of simple rheumatic or neuralgic affections. But even in cases where larger doses are required, the danger of poisoning is apparently not very great, provided the usual caution is being taken, not to begin with too large a dose. Though I do not consider salol a panacea, I do not hesitate to advocate the use of it in cases where the salicylate of sodium is indicated, than which it is safer, although in certain cases the salicylate is more effective than salol; whilst in other cases salol exhibits an action which cannot be produced by the salicylate, and which, very probably, is due to the combined action of the salicylic and carbolic acid.

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